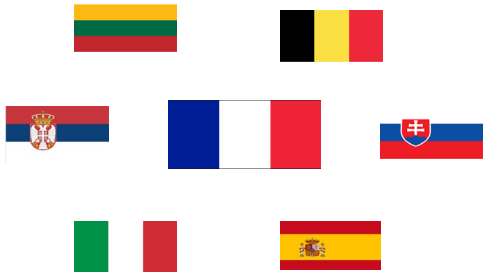
iPAAC
INNOVATIVE PARTNERSHIP
FOR ACTION AGAINST CANCER



WP9 – Current state of play

Govermental Board – 24 January 2019

Co-funded by
the Health Programme
of the European Union

INSTITUT NATIONAL DU CANCER

WP9 TASKS AND GOALS

iPAAC
INNOVATIVE PARTNERSHIP
FOR ACTION AGAINST CANCER

INNOVATIVE THERAPIES IN CANCER

1) **Map existing guidelines** and reference frameworks regarding the use of immunotherapies in clinical practices and identify potential off-label use

- Promote the proper use of these innovative treatments
- Spur coordination across institutions, professionals and Member States

2) Identify and validate predictive **biomarkers** for response, resistance or toxicity

- Better identification of responders or non responders

3) Predict impact of forthcoming innovative treatments with **horizon scanning** activities

- Anticipation of new therapies, their associated costs and their place in the therapeutic strategy

4) Identify tools that could be implemented in Europe for **real-life monitoring** of innovative treatments

- Provide guidance regarding the assessment of innovative therapies in real-life setting

Co-funded by
the Health Programme
of the European Union

WP9 SCOPE

- Innovative therapies against cancer
  - Focus on innovative immunotherapies
    - Checkpoint inhibitors
    - CAR-T cells

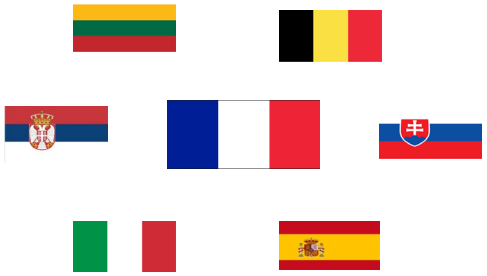
OVERVIEW OF THE TYPES OF CANCERS FOR WHICH CHECKPOINT INHIBITORS AND CAR-T CELLS HAVE (AT LEAST) ONE APPROVED THERAPEUTIC INDICATION IN THE EUROPEAN UNION (August 2018)

	CHECKPOINT INHIBITORS				
	anti-CTLA-4	anti-PD-1		anti-PD-L1	
Cancer types*	Ipilimumab (Yervoy®)	Nivolumab (Opdivo®)	Pembrolizumab (Keytruda®)	Avelumab (Bavencio®)	Atezolizumab (Tecentriq®)
Melanoma	2011	June-15	July-15		
Non-small cell lung cancer		Oct-15	Aug-16		Sept-17
Renal cell carcinoma		Apr-16			
Classical Hodgkin's lymphoma		Nov-16	May-17		
Squamous head and neck cancer		Apr-17			
Urothelial carcinoma		June-17	Aug-17		Sept-17
Merkel cell carcinoma				Sept-17	

	CAR-T CELLS	
Cancer types	Tisagenlecleucel (Kymriah®)	Axicabtagene ciloleucel (Yescarta®)
B-cell acute lymphoblastic leukaemia (ALL)	Aug-18	
large B-cell lymphoma	Aug-18	Aug-18

Co-funded by the Health Programme of the European Union

iPAAC
INNOVATIVE PARTNERSHIP
FOR ACTION AGAINST CANCER



WP9 – TASK 1

Clinical practice guidelines and reference frameworks related to the use of immunotherapies

Co-funded by
the Health Programme
of the European Union

INSTITUT NATIONAL DU CANCER

STRUCTURE OF THE WORK FOR WP9 TASK 1: 3 MAIN QUESTIONS TO ANSWER

iPAAC
INNOVATIVE PARTNERSHIP
FOR ACTION AGAINST CANCER

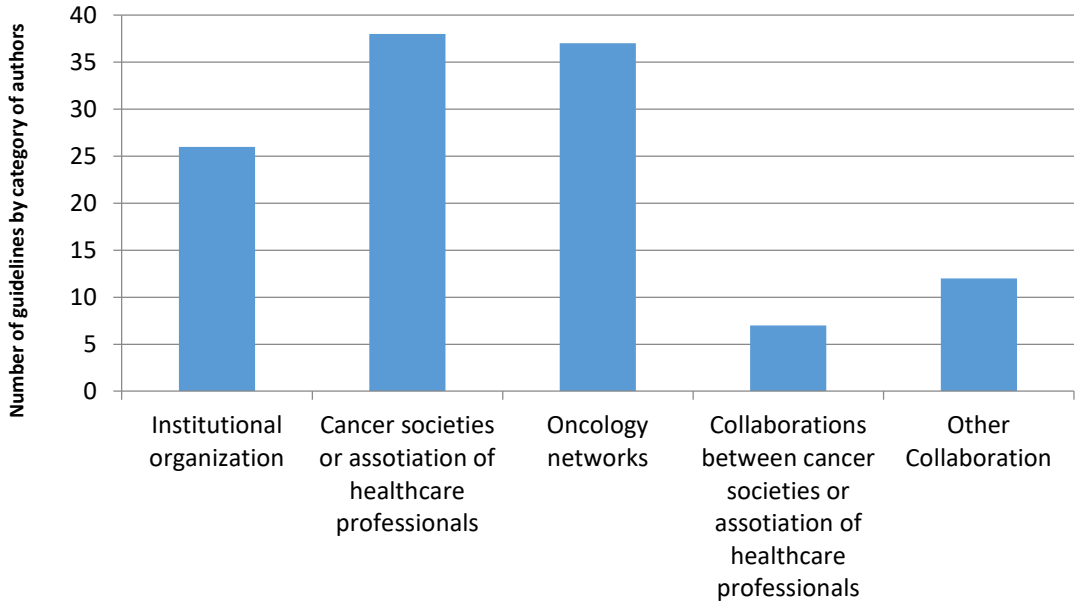
1. Innovative immunotherapies within clinical practice guidelines
   - Mapping of clinical practice guidelines
   - Place of innovative immunotherapies within guidelines
   - Off-label recommendations: why, from who, how?
2. Access to innovative immunotherapies and potential restrictions of use
   - Mapping of reference frameworks restricting the use of ITS (HTA opinion mainly)
   - Identification of restrictions of access (based on reimbursement)
   - Comparison of access to immunotherapies between European countries
3. Programs/Frameworks enabling early access to innovative immunotherapies for an unapproved indication
   - Mapping of programs/reference frameworks enabling early access to innovative immunotherapies for unapproved indication
   - Pros and cons of each program
   - Comparison of access between European countries

Co-funded by
the Health Programme
of the European Union

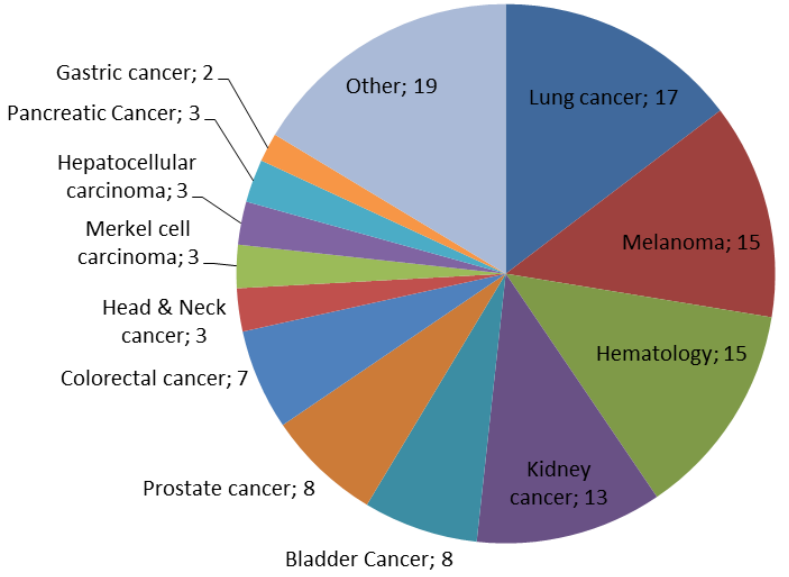
KEY RESULTS FROM TASK 1 – LITERATURE REVIEW

iPAAC
INNOVATIVE PARTNERSHIP
FOR ACTION AGAINST CANCER

- Mapping of clinical practice guidelines positionning innovative immunotherapies published in French and in English
  - More than 120 clinical practice guidelines identified (FR + EN)



Distribution of clinical practice guidelines by type of authors



Distribution of clinical practice guidelines by localization

Co-funded by the Health Programme of the European Union

MAIN CONCLUSIONS FROM LITERATURE REVIEW

iPAAC
INNOVATIVE PARTNERSHIP
FOR ACTION AGAINST CANCER

- Low visibility of national guidelines at the European level
  - Publication in local langage ➔ barrier langage
  - Only few are referenced in PubMed
- Place of innovative immunotherapies differs between guidelines
  - This could be explained by missing comparative data between several new therapies arriving at the same time on the market
- Hard to keep a document up-to-date in this fast evolving field
  - Need for more collaboration in Europe?
- Off-label recommandations identified
  - Mainly for small target groups (e.g. MSI-H tumors), or for indications already approved in other countries (e.g. USA)

➔To be further investigated with results from questionnaire addressed to clinical practice guidelines providers (ESMO, ASCO, AFU, …)

➔Examples of data which could be integrated into the Roadmap:

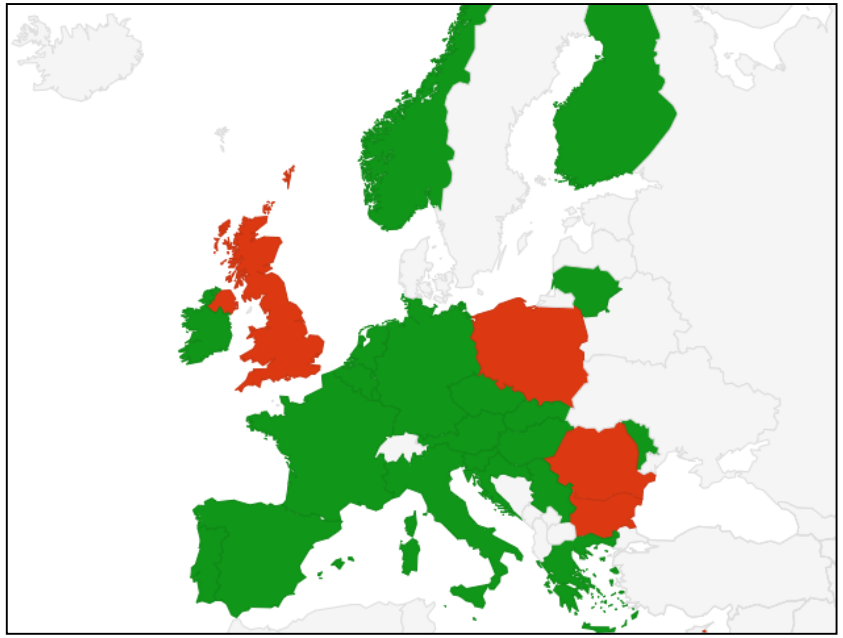
- list of clinical practice guideline providers (institutions, cancer societies, …) with available website
- Methods suggested to speed up implementation of recommandations

Co-funded by
the Health Programme
of the European Union

KEY RESULTS FROM QUESTIONNAIRE 1

iPAAC
INNOVATIVE PARTNERSHIP
FOR ACTION AGAINST CANCER

- To complete the literature review: 1 questionnaire to iPAAC partners to request information regarding:
  - Organizations writing/providing clinical practice guidelines in European countries;
  - The availability and accessibility of innovative immunotherapies in European countries, especially in terms of reimbursement;
  - Existing programs enabling early access to innovation therapies against cancer for unapproved indication.



- Completed by 23 countries between 16 Oct and 27 Nov 2018
  - 3 iPAAC associated countries missing : Bulgaria, Poland, Romania
  - 2 additional countries participating: Austria, Netherlands

- 24 answers in total (2 from Spain, from different regions)

Co-funded by
the Health Programme
of the European Union

CLINICAL PRACTICE GUIDELINES

iPAAC
INNOVATIVE PARTNERSHIP
FOR ACTION AGAINST CANCER

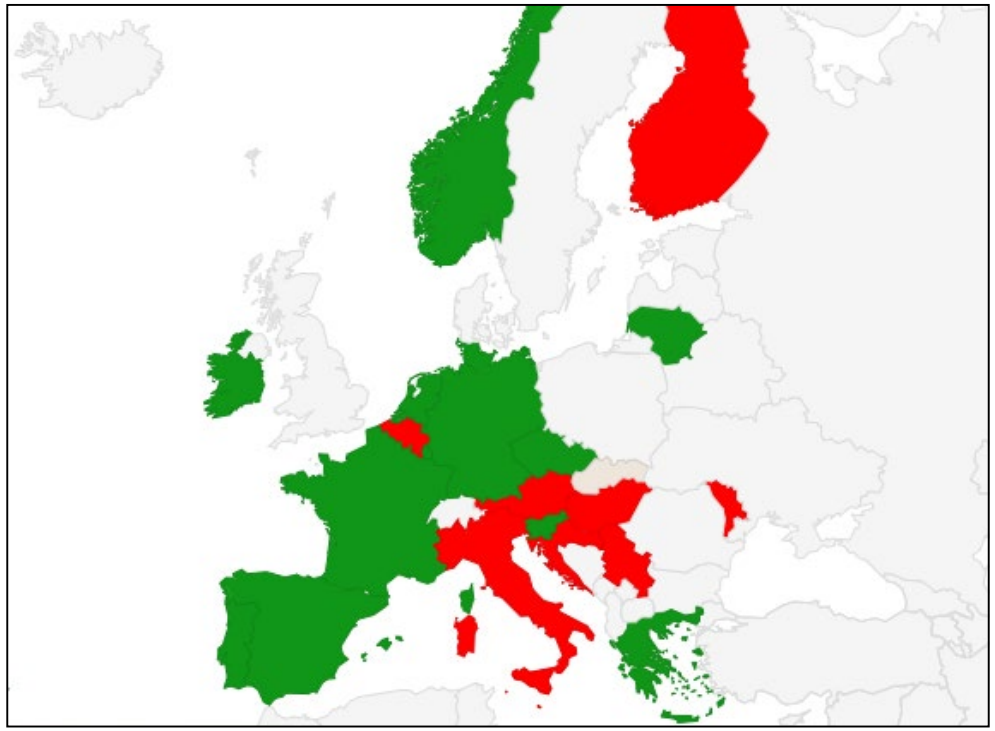
- All countries have at least one national or regional organization in charge of writing clinical practices guidelines related to oncology, **except Slovakia and Malta**.
- Most of the guidelines are written in **national language**.
- Some countries translate publications in English like Spain and Greece where respectively the Spanish and the Hellenic societies for medical oncology translate their guidelines in English. In other countries like Belgium, France, Germany, guidelines sometimes have related publication in scientific papers in English

Co-funded by
the Health Programme
of the European Union

PLACE OF INNOVATIVE IMMUNOTHERAPIES IN CPG

iPAAC
INNOVATIVE PARTNERSHIP
FOR ACTION AGAINST CANCER

- Only half of the countries (12/23, 52%) have included innovative immunotherapies in the treatment strategy in at least one clinical practice guideline related to oncology



- First Marketing Authorization for checkpoint inhibitors is from 2011; nivolumab and pembrolizumab from 2015
  - ➔ still quite a delay to implement these new therapies into clinical practice guidelines
  - ➔ Need to improve timelines for production and update of guidelines including innovative therapies

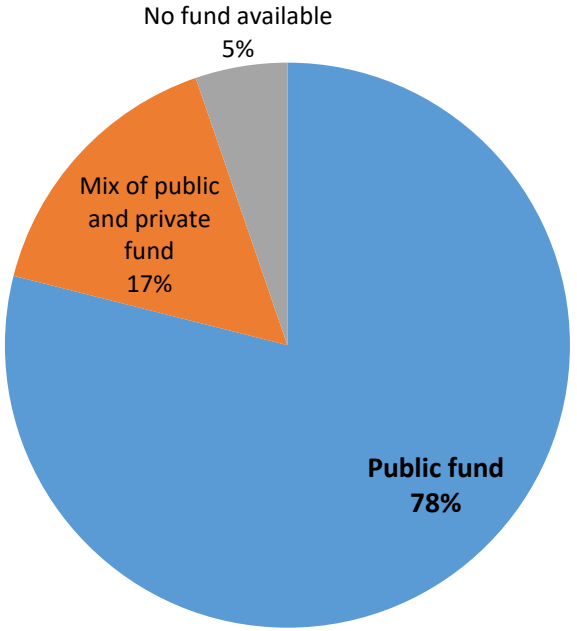
Co-funded by
the Health Programme
of the European Union

ACCESS AND FINANCING OF INNOVATIVE THERAPIES

iPAAC
INNOVATIVE PARTNERSHIP
FOR ACTION AGAINST CANCER

- Most of the countries who participated to the questionnaire have a public fund available to finance these innovative immunotherapies
  - No fund available : Moldova
  - Mix of public and private:

  Lithuania, Norway, Ireland



- In countries where there is a public fund available, there are no out-of-pocket costs for patients

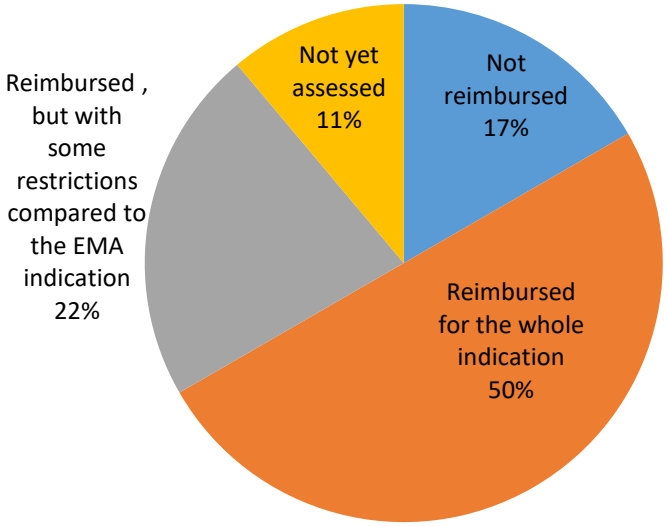
Co-funded by
the Health Programme
of the European Union

AVAILABILITY OF IMMUNOTHERAPIES IN TERMS OF REIMBURSEMENT - MELANOMA

iPAAC
INNOVATIVE PARTNERSHIP
FOR ACTION AGAINST CANCER

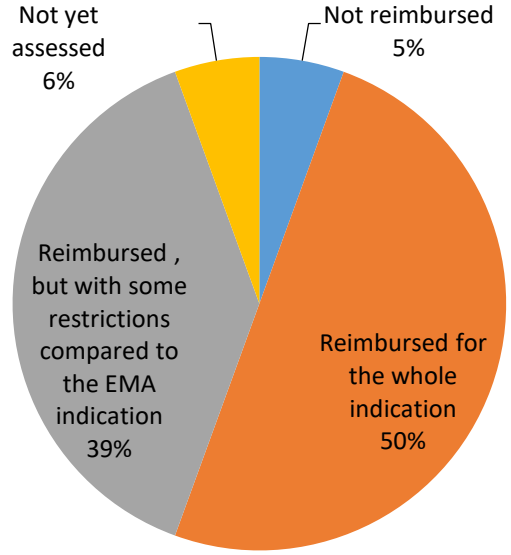
YERVOY (ipilimumab)

as monotherapy is indicated for the treatment of advanced (unresectable or metastatic) melanoma in adults, and adolescents 12 years of age and older



OPDIVO (nivolumab)

as monotherapy or in combination with ipilimumab is indicated for the treatment of advanced (unresectable or metastatic) melanoma in adults.



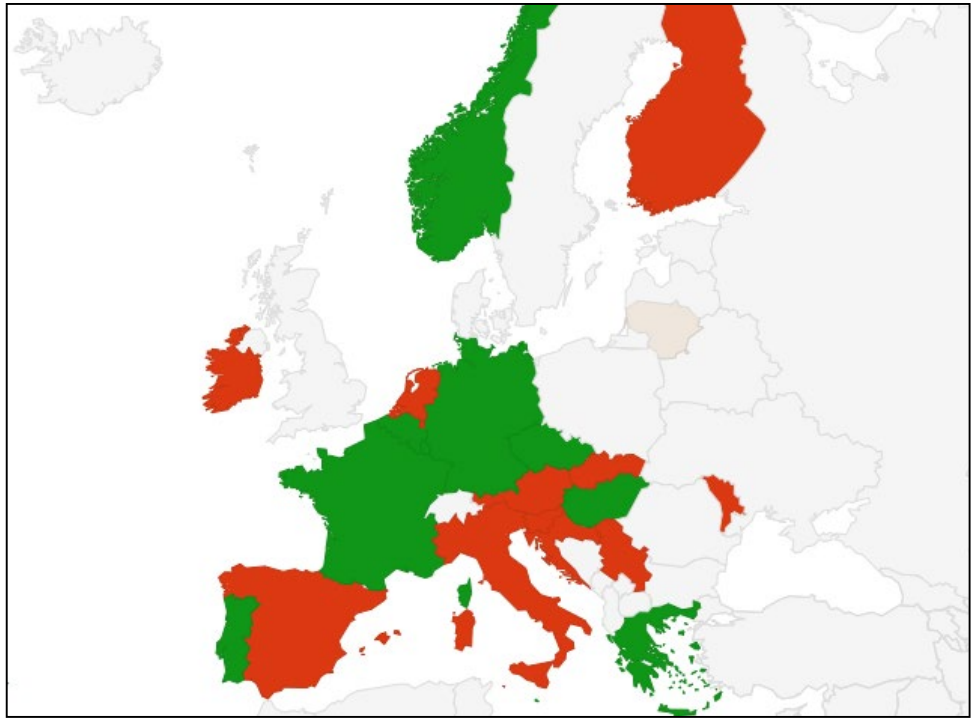
Exemples of reimbursement restriction: In Portugal, nivolumab is reimbursed for the treatment of unresectable or metastatic melanoma in adults **only for BRAF wild patients**, with ECOG 0 and 1 and no active brain metastasis

Co-funded by
the Health Programme
of the European Union

EARLY ACCESS PROGRAMS (I)

iPAAC
INNOVATIVE PARTNERSHIP
FOR ACTION AGAINST CANCER

- About half of the countries (10/22, 45%) mentioned that they have an existing program enabling early access to innovation therapies against cancer (before marketing authorization or before extension of indication)



Note: N = 22 countries
(no reply received from Lithuania on this topic)

➔ *A Brief description of each early access program identified could be shared within the Roadmap*

Co-funded by
the Health Programme
of the European Union

OPINION OF EUROPEAN STAKEHOLDERS ON ACCESS TO INNOVATIVE IMMUNOTHERAPIES

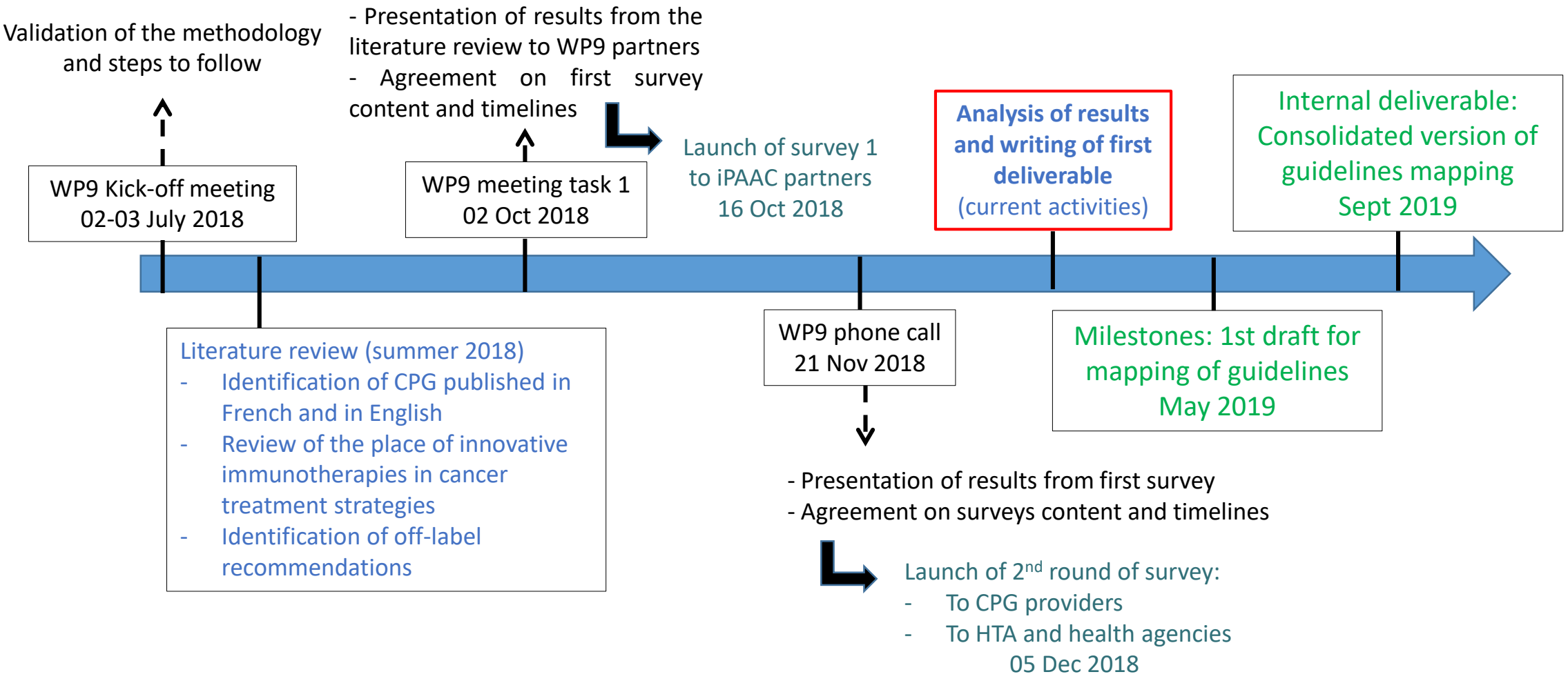
iPAAC
INNOVATIVE PARTNERSHIP
FOR ACTION AGAINST CANCER

- This questionnaire will be distributed to:
  - HTA agencies
  - Health/medicine agencies
    - For some organizations, only the generic email address is available: it might be harder to get a reply: any additional contacts identified?
  - Patients
    - Through ECPC
  - Healthcare professionals
    - Cancer societies will receive the questions which are also included in the 1st questionnaire

Co-funded by
the Health Programme
of the European Union

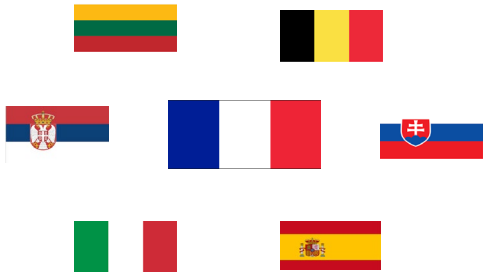
TIMELINES / MILESTONES TASK 1

iPAAC
INNOVATIVE PARTNERSHIP
FOR ACTION AGAINST CANCER



Co-funded by the Health Programme of the European Union

iPAAC
INNOVATIVE PARTNERSHIP
FOR ACTION AGAINST CANCER



WP9 – TASK 2

Biomarkers

Co-funded by
the Health Programme
of the European Union

INSTITUT NATIONAL DU CANCER

BIOMARKERS

iPAAC
INNOVATIVE PARTNERSHIP
FOR ACTION AGAINST CANCER

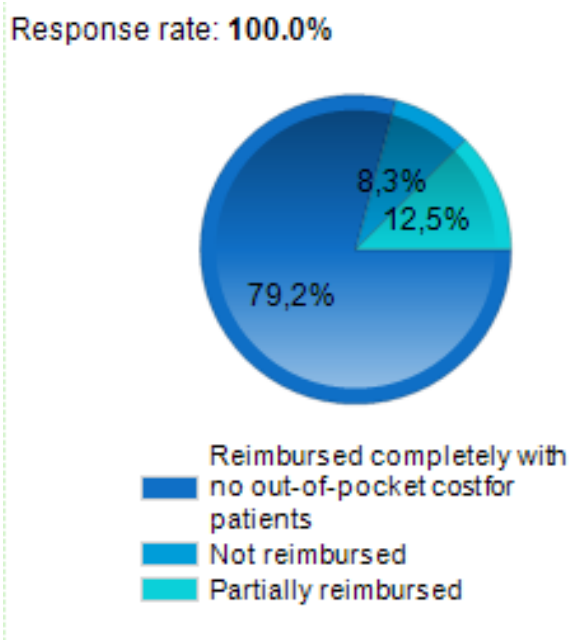
- Fully integrated in task 1 & 3
- For the next meeting planned on 06 March 2019
  - Summary of main biomarkers identified will be prepared
    - PD-L1 expression
    - MSI-H
    - TMB
    - BRAF status (conditioning the potential presciption of some anti-PD-1)

Co-funded by
the Health Programme
of the European Union

REIMBURSEMENT OF BIOMARKER EXPRESSION TESTS

iPAAC
INNOVATIVE PARTNERSHIP
FOR ACTION AGAINST CANCER

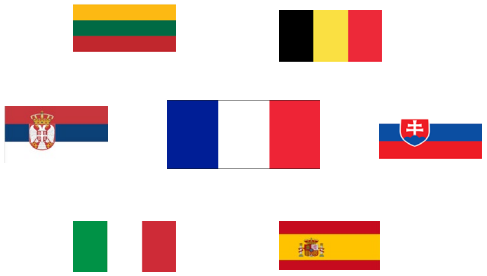
- When the prescriptions of immunotherapies are conditioned by the prerequisite of a specific biomarker expression, is the molecular test to assess the biomarker reimbursed in your country?



Note: For Spain, the reimbursement might varies depending on the region

Co-funded by
the Health Programme
of the European Union

iPAAC
INNOVATIVE PARTNERSHIP
FOR ACTION AGAINST CANCER



WP9 – TASK 3

Horizon Scanning Activities

Co-funded by
the Health Programme
of the European Union

INSTITUT NATIONAL DU CANCER

TASK 3 – STATE OF WORK

iPAAC
INNOVATIVE PARTNERSHIP
FOR ACTION AGAINST CANCER

- Preparation of the next meeting: 06 March 2019 in Brussels
  - Important organizations involved in Horizon scanning activities will be represented:
    - HS networks: Euroscan and IHSI/BeNeLuxA
    - NICE
    - Ludwig Boltzmann institute from Austria
    - EUnetHTA (?)
  - The aim of this meeting will be to:
    - Agree on the content and steps to follow for the retrospective analysis
    - Panel discussion around collaborations in this field and how to limit inequalities in Europe

Co-funded by
the Health Programme
of the European Union

TIMELINES / MILESTONES TASK 3

iPAAC
INNOVATIVE PARTNERSHIP
FOR ACTION AGAINST CANCER

WP9 Kick-off meeting
02-03 July 2018

WP9 meeting task 2 & 3
06 March 2019

Milestones: 1st draft
November 2019

April 2020
Internal deliverable regarding
Horizon scanning in Europe

Preparation of the task
- Literature review
- Meetings with Euroscan, IHSI

Retrospective analysis to evaluate the efficiency of HS in oncology

- Highlight specific features needed in HS systems for
  - cell and gene therapies
  - Biomarkers
- Assessment of inequalities between European Countries

Review of existing Horizon scanning systems and organizations

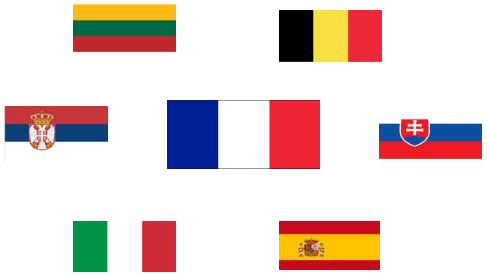
eunethta
EuroScan International Network
Canadian Agency for Drugs and Technologies in Health
BeNeLuxA

Identification of key figures and issues associated with innovative cancer therapies

OECD
FDA
EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Co-funded by
the Health Programme
of the European Union

iPAAC
INNOVATIVE PARTNERSHIP
FOR ACTION AGAINST CANCER



WP9 – TASK 4

Real-life monitoring of innovative immunotherapies

Co-funded by
the Health Programme
of the European Union

INSTITUT NATIONAL DU CANCER

iPAAC
INNOVATIVE PARTNERSHIP
FOR ACTION AGAINST CANCER

Any questions/suggestions?

Co-funded by
the Health Programme
of the European Union